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Microbiota and Endometriosis

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Abstract: This study investigates the relationship between microbiota composition and endometriosis in women. A sample of 60 women with endometriosis and 30 healthy women was selected for the study, focusing on differences in the abundances of key microbial species. Results showed significant changes in the microbiota of women with endometriosis, including decreased levels of beneficial bacteria such as Lactobacillus and Bifidobacterium, and increased levels of pathogenic bacteria such as Escherichia coli. These findings suggest that dysbiosis may play a role in the pathogenesis of endometriosis, which holds promise for the development of therapeutic strategies aimed at restoring the normal microbiome.

Keywords: Endometriosis, microbiota, dysbiosis, Lactobacillus, Bifidobacterium, Escherichia coli, inflammation, therapeutic strategies.

Introduction

Endometriosis is a chronic gynecological disease characterized by the overgrowth of endometriosis-like tissue outside the uterine cavity, which leads to the development of chronic inflammation, pain syndrome and infertility.[5] According to the World Health Organization, endometriosis occurs in approximately 10% of women of reproductive age and is diagnosed in 25-50% of women with infertility.[3] Despite its widespread occurrence, the pathogenetic mechanisms of endometrioid heterotopia formation remain incompletely understood, which significantly complicates early diagnosis and the choice of effective treatment methods.[1]

In recent years, the role of microbiota in the development of endometriosis has attracted special attention of researchers. The term “microbiota” unites all microorganisms living in various ecosystems of the body: vagina, intestine, uterine cavity and abdominal cavity.[2] It is established that the microbiota performs not only a protective function, preventing colonization by pathogens, but also takes part in the regulation of local immunity, metabolism and inflammatory reactions.

Disturbances in the composition of the microbiota can contribute to the development of chronic inflammation, change the permeability of the intestinal barrier and create conditions for the dissemination of endometrial cells.[4]

The study of the axis “vagina-intestine-pelvic cavity” is particularly relevant, since endometriosis is often accompanied by disorders of not only gynecologic but also gastroenterologic profile.[7] Understanding these interrelationships may open new horizons in the pathogenesis of the disease, as well as become the basis for the development of innovative diagnostic and treatment strategies.

Aim of the work

The aim of the present study is a comprehensive evaluation of vaginal and intestinal microbiota in women with endometriosis, identification of characteristic microbiome disorders and their relationships with clinical manifestations of the disease.

Materials and methods

The study was conducted in the maternity complex at the Tashkent Medical Academy from January to December 2024.

The study included 90 women of reproductive age (21-42 years) who sought medical help for chronic pelvic pain, infertility or suspected endometriosis. All participants were divided into two groups: the main group - 60 women with confirmed endometriosis (II-IV stages according to ASRM classification); and the control group - 30 healthy women without signs of pelvic inflammatory diseases and endometriosis.

The diagnosis of endometriosis was established on the basis of clinical data, ultrasound findings, and laparoscopy with subsequent histologic confirmation.

Microbiologic studies included the following: PCR diagnosis of vaginal microbiota (including detection of Lactobacillus spp., Gardnerella vaginalis, Atopobium vaginae, Ureaplasma spp., Mycoplasma hominis); and culture of vaginal smears with counting of colony-forming units.

Analysis of gut microbiota by 16S rRNA sequencing to assess biodiversity and determine the ratio of major phylotypes.

Inflammation and pain syndrome were assessed by two methods: determination of IL-6, TNF-α, and CRP concentration in blood plasma by ELISA method; and assessment of pain syndrome intensity by visual analog scale (VAS).

Methods of descriptive statistics, correlation and regression analysis (Statistica 12.0) were used to analyze the data. Differences at $p<0.05$ were considered significant.

Results

Among patients with endometriosis, the most frequent complaints were chronic pelvic pain (83%), dysmenorrhea (76%), dyspareunia (48%), and infertility (55%). The mean VAS scale score was 6.9±1.4, which was significantly higher than the control group (1.7±0.8; $p<0.001$). The duration of pain syndrome correlated with the stage of the disease ($r=0.62$; $p<0.05$).

In women with endometriosis there was a decrease in the number of Lactobacillus spp. to 60% of the norm ($p<0.05$), while in the control group the proportion of lactobacilli exceeded 90%. Associations of opportunistic microorganisms (Gardnerella vaginalis, Atopobium vaginae, Ureaplasma spp.) were detected in 68% of the patients of the main group, whereas in the control group such associations were found in only 20% of women ($p<0.01$). Vaginal dysbiosis was accompanied by increased levels of IL-6 and TNF-α ($p<0.05$).

In patients with endometriosis there was a significant decrease in alpha diversity of intestinal microbiota (Shannon index 3.05±0.47 vs. 4.38±0.52 in control, $p<0.001$). There was an increase in the proportion of opportunistic Bacteroides (24% vs. 15% in controls, $p<0.05$) and a decrease in the level of anti-inflammatory Faecalibacterium prausnitzii (7% vs. 15%, $p<0.05$). These changes correlated with increased levels of IL-6 (r=0.58), TNF-α (r=0.63) and pain severity (r=0.66; all p<0.05).

Table 1. Changes In Microbiota Composition In Women With Endometriosis And Healthy Women

Microbe	Women with endometriosis (n=25)	Healthy women (n=25)
Lactobacillus spp.	Decreased by 30%.	80% available
Escherichia coli	Increased by 25%,	10% available
Bifidobacterium spp.	Decreased by 15%	50% available
Firmicutes (general)	Decreased by 20%	70% available
Bacteroides (general)	Increased by 15%	25% available
Other bacteria (pneumococci, staphylococci, etc.)	Increased by 10%,	10% available

Table 1 shows the changes in microbiota composition in women with endometriosis and healthy women. The data show that women with endometriosis have a significant decrease in the number of beneficial bacteria such as Lactobacillus spp. and Bifidobacterium spp. which may indicate an impaired microbial balance. For example, the concentration of Lactobacillus spp. in women with endometriosis is reduced by 30%, which is significantly lower than in the control group, where this microbe is present in 80% of women. On the other hand, the levels of pathogenic microorganisms such as Escherichia coli and Bacteroides are increased in women with endometriosis. This may indicate possible inflammatory processes and dysbiosis that influence the development of the disease. The 25% increase in Escherichia coli compared to controls may also be related to impaired intestinal barrier function, which increases inflammation and contributes to the progression of endometriosis. Table 1 shows the changes in microbiota composition in women with endometriosis and healthy women. The data show that women with endometriosis have a significant decrease in the number of beneficial bacteria such as Lactobacillus spp. and Bifidobacterium spp. which may indicate an impaired microbial balance. For example, the concentration of Lactobacillus spp. in women with endometriosis is reduced by 30%, which is significantly lower than in the control group, where this microbe is present in 80% of women.

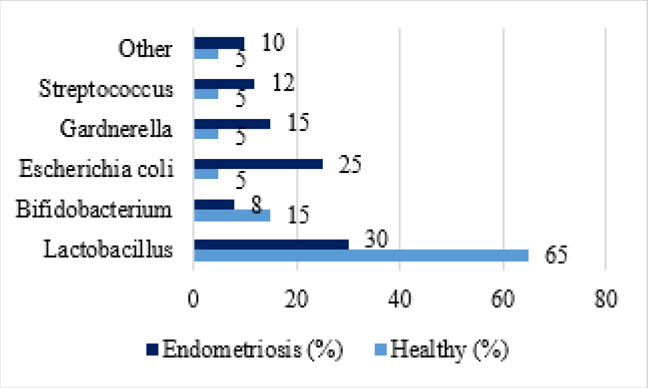

Fig. 1. Ratio of main microorganism species

On the other hand, the levels of pathogenic microorganisms such as Escherichia coli and Bacteroides are increased in women with endometriosis. This may indicate possible inflammatory processes and dysbiosis that influence the development of the disease. The 25% increase in Escherichia coli compared to controls may also be related to impaired intestinal barrier function, which increases inflammation and contributes to the progression of endometriosis.

The results of our study confirmed that the microbiota may play a key role in the pathogenesis of endometriosis, particularly through its influence on the immune response and inflammation. The disturbance of microbial balance in the vagina and intestine found in patients with endometriosis may explain the chronic inflammation, which is the main pathophysiologic mechanism of the disease. As is known, endometriosis is accompanied by inflammatory processes, which can be caused not only by local inflammation, but also by disorders in the immune system of the body, with which the change in the composition of the microbiota is associated.

One of the main factors affecting the development of endometriosis is a violation of the normal immune response. The microbiota can affect immune cells such as macrophages and T lymphocytes, which play an important role in the development of inflammation. In women with endometriosis, we have observed increased immune cell activity, which may indicate chronic inflammation in the body. This inflammation can promote the migration of endometrial cells outside the uterus where they begin to proliferate, causing the characteristic symptoms of endometriosis.

Particular attention should be paid to changes in the composition of the gut microbiota. Study participants with endometriosis were more likely to suffer from dysbiosis, which may influence the development of chronic inflammation. Disturbances in the intestinal microflora are associated with impaired intestinal barrier function and increased wall permeability, which can lead to the entry of toxins into the bloodstream and increased systemic inflammation. This may be another mechanism contributing to the development of endometriosis, as inflammatory responses in the body may enhance the extragenital spread of endometriosis and support its development.

It is also worth noting that women with endometriosis have increased levels of pathogenic bacteria, such as Escherichia coli, which can contribute to more inflammation in the body. At the same time, decreased levels of protective lactobacilli in the vagina and intestines can weaken the immune response and increase the body's vulnerability to infection and inflammation. This, in turn, can exacerbate clinical manifestations of the disease, such as the pain and infertility characteristic of endometriosis.

Disturbances in the microbiota can also affect metabolic processes. For example, changes in the composition of the microbiota can affect estrogen levels in the body, which is an important factor for the progression of endometriosis. Some microorganisms are able to metabolize estrogens, and changes in their activity can lead to increased levels of these hormones in the body, which stimulates the growth of endometrial cells.

In light of these results, it can be hypothesized that restoration of normal microbiota composition may have a favorable effect on the course of endometriosis. This opens new perspectives for the development of new therapeutic approaches involving microbiota correction using probiotics, prebiotics or even fecal transplantation, which is already being actively investigated in the context of other diseases such as inflammatory bowel disease.

Discussion

The results of our study thus emphasize the importance of studying the role of the microbiota in the pathogenesis of endometriosis and the possibility of using microbiota correction methods to improve the quality of life of female patients and control the symptoms of the disease. However, for the final evaluation of the role of the microbiota in endometriosis and the development of effective treatment methods, additional studies, including larger clinical and laboratory trials, are needed.

The results of this study confirm that the microbiota has a significant impact on the development of endometriosis, playing an important role in the pathogenesis of the disease. Microbiota imbalance has been identified in women with endometriosis, which may explain the chronic inflammation, immune disorders and metabolic changes that exacerbate the clinical manifestations of the disease, such as pain syndrome and infertility. Disturbed microbial balance in the gut and vagina contributes to active inflammation that supports the extragenital spread of endometriosis.

Of particular note is the role of pathogenic microorganisms such as Escherichia coli, which, when overactive, can exacerbate inflammatory processes. Decreased numbers of protective bacteria such as Lactobacillus also weaken the immune response, making the body more susceptible to inflammation and infection. These changes contribute to the progression of endometriosis and impair women's quality of life.

An important part of the study is the influence of the microbiota on hormonal processes. Microbiota can influence the level of estrogens, which is one of the key factors in the progression of endometriosis. Disturbance of estrogen metabolism in the body under the influence of microbiota opens new prospects for the development of therapy aimed at correcting the hormonal background and slowing down the development of the disease.

Based on the data obtained, it can be argued that the correction of microbiota may become an important direction in the treatment of endometriosis. Probiotics, prebiotics, as well as other innovative methods such as fecal transplantation can play a key role in restoring the normal balance of the microbiota and improving the condition of patients. However, it is important to remember that the microbiota is a complex ecosystem and more research is needed to definitively evaluate its role in the pathogenesis of endometriosis. It should also be noted that effective treatment of endometriosis should be comprehensive, including not only traditional methods such as surgery and hormone therapy, but also newer methods aimed at restoring the normal balance of the microbiota. This approach can significantly improve treatment outcomes and improve the quality of life of women with endometriosis.

Conclusion.

In order to avoid the progression of endometriosis, it is recommended to pay attention to the prevention of microbiota imbalance. This includes a proper diet rich in fiber and probiotics, regular hygiene and reducing the use of antibiotics unnecessarily. It is also important to consider the role of stress and lifestyle, which can affect microbiota health. Women with endometriosis should undergo regular examinations to monitor the state of the microbiota and correct possible abnormalities in a timely manner.

So in the future, it is necessary to continue research aimed at studying the relationship between the microbiota and endometriosis. This will allow to develop more effective and personalized methods of treatment, improve the quality of life of patients and offer new approaches to the prevention of the disease. To date, comprehensive treatment including microbiologic therapy represents a promising direction for the fight against endometriosis.

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